Effectiveness and Acceptability of Cognitive Behavior Therapy Delivery Formats in Adults with Depression

Cuijpers, Pim; Noma, Hisashi; Karyotaki, Eirini; Cipriani, Andrea; Furukawa, Toshi A.

published in
JAMA Psychiatry
2019

DOI (link to publisher)
10.1001/jamapsychiatry.2019.0268

document version
Publisher's PDF, also known as Version of record

JAMA Psychiatry | Original Investigation

Effectiveness and Acceptability of Cognitive Behavior Therapy Delivery Formats in Adults With Depression
A Network Meta-analysis

Pim Cuijpers, PhD; Hisashi Noma, PhD, MD; Eirini Karyotaki, PhD; Andrea Cipriani, PhD, MD; Toshi A. Furukawa, PhD, MD

IMPORTANCE Cognitive behavior therapy (CBT) has been shown to be effective in the treatment of acute depression. However, whether CBT can be effectively delivered in individual, group, telephone-administered, guided self-help, and unguided self-help formats remains unclear.

OBJECTIVE To examine the most effective delivery format for CBT via a network meta-analysis.

DATA SOURCES A database updated yearly from PubMed, PsycINFO, Embase, and the Cochrane Library. Literature search dates encompassed January 1, 1966, to January 1, 2018.

STUDY SELECTION Randomized clinical trials of CBT for adult depression. The 5 treatment formats were compared with each other and the control conditions (waiting list, care as usual, and pill placebo).

DATA EXTRACTION AND SYNTHESIS PRISMA guidelines were used when extracting data and assessing data quality. Data were pooled using a random-effects model. Pairwise and network meta-analyses were conducted.

MAIN OUTCOMES AND MEASURES Severity of depression and acceptability of the treatment formats.

RESULTS A total of 155 trials with 15 191 participants compared 5 CBT delivery formats with 2 control conditions. In half of the studies (78 [50.3%]), patients met the criteria for a depressive disorder; in the other half (77 [49.7%]), participants scored above the cutoff point on a self-report measure. The effectiveness of individual, group, telephone, and guided self-help CBT did not differ statistically significantly from each other. These formats were statistically significantly more effective than the waiting list (standardized mean differences [SMDs], 0.87-1.02) and care as usual (SMDs, 0.47-0.72) control conditions as well as the unguided self-help CBT (SMDs, 0.34-0.59). In terms of acceptability (dropout for any reason), individual (relative risk [RR] = 1.44; 95% CI, 1.09-1.89) and group (RR = 1.38; 95% CI, 1.06-1.80) CBT were significantly better than guided self-help. Guided self-help was also less acceptable than being on a waiting list (RR = 0.63; 95% CI, 0.52-0.75) and care as usual (RR = 0.72; 95% CI, 0.57-0.90). Sensitivity analyses supported the overall findings.

CONCLUSIONS AND RELEVANCE For acute symptoms of depression, group, telephone, and guided self-help treatment formats appeared to be effective interventions, which may be considered as alternatives to individual CBT; although there were few indications of significant differences in efficacy between treatments with human support, guided self-help CBT may be less acceptable for patients than individual, group, or telephone formats.

Editorial page 678

Author Audio Interview

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Pim Cuijpers, PhD, Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health Research Institute, Vrije Universiteit Amsterdam, Van der Boechorststraat 7-9, 1081 BT Amsterdam, the Netherlands (p.cuijpers@vu.nl).

JAMA Psychiatry. 2019;76(7):700-707. doi:10.1001/jamapsychiatry.2019.0268
Published online April 17, 2019.Corrected on July 17, 2019.

Randomized clinical trials have shown that cognitive behavior therapy (CBT) is effective in treating depression[1,2] and at least as effective as any other type of psychotherapy.[1,3] Although CBT was developed as an individual therapy,[4] it is also available as a group, telephone-administered, and self-help therapy in which patients work through a standardized protocol independently. The protocol can be in book format or available on the internet. Self-help therapy can either be guided (ie, involving a professional therapist) or unguided (ie, providing no professional guidance to the patient using the materials).

Many meta-analyses have examined these CBT delivery formats.[5-14] Overall, the effects of individual, group, telephone-administered, and guided self-help (internet based or not) formats seem to be comparable in magnitude to the control conditions, whereas the unguided self-help format seems to make a small but substantial difference and to be less effective than the individual, group, telephone, and guided self-help formats.

However, conventional pairwise meta-analyses can only compare 2 treatment formats at a time, and only through network meta-analysis can we examine all formats simultaneously in a single analysis. Because network meta-analysis can combine direct and indirect evidence, it can assess the relative effectiveness of the different CBT delivery formats. To date, no previous network meta-analysis has examined these treatment formats.

Key Points

Question Which cognitive behavior therapy delivery format is most effective and acceptable for the treatment of acute depression?

Findings In this network meta-analysis of 155 trials involving 15 191 patients, no statistically significant differences in effectiveness were found among individual, group, telephone, and guided self-help treatment formats, although acceptability may be somewhat lower for guided self-help format. Unguided self-help therapy was not more effective than care as usual.

Meaning For acute symptoms of depression, group, telephone-administered, and guided self-help (internet-based or not) cognitive behavior therapy appeared to be effective and may be considered as alternatives to individual therapy.

Methods

Identification and Selection of Studies

We used a database of randomized clinical trials examining the psychological treatment of depression. The database is continuously updated and was developed through a comprehensive literature search from January 1, 1966, to January 1, 2018 by two of us (P.C. and E.K.), of PubMed, PsycINFO, Embase, and the Cochrane Library. The search used a combination of index and text words indicative of depression and psychotherapies and set filters for randomized clinical trials (eAppendix A in the Supplement shows the full search string for PubMed). All records were screened by 2 independent researchers (P.C. and E.K.), and all studies that could possibly meet the inclusion criteria according to one of the researchers were retrieved as full text. The decision to include or exclude a study was also made by 2 independent researchers (P.C. and E.K.). Disagreements were solved through discussion. The network meta-analysis is registered in the PROSPERO as CRD42017064442.

We defined CBT as a therapy in which cognitive restructuring was one of the core components.[1-3] Cognitive restructuring is aimed at evaluating, challenging, and modifying a patient's dysfunctional beliefs.

We included studies in which CBT was examined in the following formats: individual, group, telephone, guided self-help (administered through the internet or other media, such as a book), and unguided self-help (internet-based or not). For the control groups, we included waiting list, care as usual, and pill placebo. The group who received care as usual while waiting was classified under the waiting list control condition. Studies were included if they compared one treatment format with another format or with one of the control conditions. Studies in which the means and SDs (or SEs or 95% CIs of means) were not reported were excluded.

Depression could be established with a diagnostic interview or with a score above a cutoff point on a self-report measure. Comorbid mental or somatic disorders were included. Studies that included patients with anxiety also were excluded, as were studies on patients with depression and comorbid substance use disorders, studies on inpatients, and studies involving adolescents or children. We also excluded maintenance studies aimed at people who had already (partly) recovered after an earlier treatment, studies in which mixed treatment formats were used (eg, both individual and group therapy), and studies on third-wave therapies. We did not set a maximum or minimum on the length of treatment.[1]

Risk of Bias and Data Extraction

Two independent researchers (P.C. and E.K.) assessed the validity of included studies using 4 criteria of the risk-of-bias assessment tool from the Cochrane Collaboration[15]: adequate generation of allocation sequence; concealment of allocation to conditions; prevention of knowledge of the allocated intervention (masking of assessors); and dealing with incomplete outcome data, which was assessed as positive when intention-to-treat analyses (ie, meaning all randomized patients were included) were conducted. Disagreements were solved through discussion.

In addition, we coded participant characteristics (ie, depressive disorder or high score on a self-rating scale, recruitment method, and target group), the number of treatment sessions, and the country in which the study was conducted.

Outcomes

We selected 1 outcome measure for each study that indicated the severity of depression using an algorithm: Hamilton Rating Scale for Depression[16]; Beck Depression Inventory I or II[17,18]; another clinician-rated instrument; another self-report instrument, with priority for the Patient Health Questionnaire 9[19];

the Center for Epidemiologic Studies–Depression Scale[20]; and the Hospital Anxiety and Depression Scale–Depression.[21] Acceptability of the treatment formats was operationalized as study dropout for any reason during the acute-phase treatment.[22]

Statistical Analysis

We conducted a series of pairwise meta-analyses for all direct comparisons using a random-effects pooling model. As an assessment of the homogeneity of effect sizes, we calculated the I^2 statistic, which is an indicator of heterogeneity in percentages, as well as τ^2. We calculated 95% CIs around the I^2 statistic using the noncentral χ^2-based approach within the Heterogi module for Stata (StataCorp).[23,24] We tested for publication bias using Egger test of the intercept to quantify the bias captured by the funnel plot and to test whether it was statistically significant.

The comparative effectiveness was evaluated using the network meta-analysis methodology of combining direct and indirect evidence for all relative treatment effects. First, we summarized the geometry of the network of evidence using network plots.[25] Second, we conducted a network meta-analysis of the comparative efficacy or acceptability using the contrast-based network meta-analysis methods.[26] Given the expected clinical and methodological heterogeneity of treatment effects among the studies, we adopted the random-effects model.[27] Comparative standardized mean differences (SMDs) and relative risks (RR) were reported with their 95% CIs and 95% prediction intervals (PrI). The PrI indicates the range in which the true effect size of 95% of all populations will fall. The ranking of treatment formats was estimated according to the surface under the cumulative ranking curve, which is based on the estimated random-effects models.[25]

In examining the transitivity assumption, we created a table of important trial and patient characteristics to verify if potential effect modifiers were similarly distributed across the comparisons in the network. We checked the consistency of the network using local and global inconsistency tests. The local inconsistency test evaluates the loop inconsistency of all the triangle loops on the network.[28] The global inconsistency is a goodness-of-fit test using the design-by-treatment interaction model of Higgins et al.[29] If any relevant sources of bias were found, we performed sensitivity analyses of how these factors were associated with the overall results.

Furthermore, we conducted a multivariate meta-regression analysis of the possible sources of heterogeneity with the same variables that were used to examine the transitivity assumption. We also examined the results at follow-up and focused on 3 to 12 months of follow-up (only a few studies examined longer follow-up periods). If a study reported several outcomes between 3 and 12 months, we selected the effect size at the latest follow-up period.

We conducted a series of 3 sensitivity analyses: one in which we included only the studies with a low risk of bias, one in which we excluded outliers (the 95% CI around the effect size did not overlap with the pooled effect size), and one in which we included only internet-based guided and unguided self-help formats (and excluded other types of self-help CBT).

We assessed the certainty of evidence in network estimates of the main outcome using the Grading of Recommendations Assessment, Development, and Evaluation framework.[30]

Most analyses were conducted in Stata/SE, version 14.2 for Mac (StataCorp). The meta-regression analyses of small sample bias were conducted in OpenBUGS, version 3.2.3 (OpenBUGS Foundation), and the Grading of Recommendations Assessment, Development, and Evaluation ratings were conducted in CINeMA.[31]

Results

Selection, Inclusion, and Characteristics of Studies

After examining a total of 19 982 abstracts (15 598 after removal of duplicates), we retrieved 2343 full-text papers for further consideration and excluded 2181 papers. The PRISMA flowchart describing the inclusion process, including the reasons for exclusion, is presented in eAppendix B in the Supplement. In total, 155 studies with 15 191 patients met the inclusion criteria. Two studies had 2 CBT interventions that met the inclusion criteria[32,33] and underwent separate comparisons. Selected characteristics of the included studies are given in eAppendix C and the references in eAppendix D in the Supplement.

The 155 studies included 57 individual, 45 group, 46 guided self-help, 10 telephone, and 21 unguided self-help arms as well as 71 waiting list, 71 care as usual, and 2 pill placebo arms. In half of the studies (78 [50.3%]), patients met the criteria for a depressive disorder; in the other half (77 [49.7%]), participants scored above the cutoff point on a self-report measure. Patients were partly recruited from the community in 77 studies (49.7%), exclusively from clinical samples in 33 studies (21.3%), and through other methods in 45 (29.0%). Seventy-eight studies (50.3%) were aimed at unselected adults, 31 (20.0%) at patients with comorbid general medical disorders, 13 (8.4%) at older adults, 11 (7.1%) at women with postpartum depression, and 22 (14.2%) at other specific target groups. Most studies (133 [85.8%]) were conducted in Western countries.

With regard to risk of bias, 92 studies (59.4%) reported an adequate sequence generation, 85 (54.8%) reported allocation to conditions by an independent or third party, 37 (23.9%) used blinded outcome assessors, and 107 (69.0%) used only self-report outcomes. In 102 studies (65.8%), intent-to-treat analyses were conducted. Sixty-one studies (39.4%) met all quality criteria, 58 (37.4%) met 2 or 3 of the criteria, and the remaining 36 (23.2%) met no or only 1 criterion.

Network Plot

The network is shown in **Figure 1**. **Table 1** shows the number of studies for each comparison. In the network plot, the nodes and edges are weighted according to the number of available treatment formats and comparisons. Overall, the network was well connected. The most examined comparisons were between individual, group, and guided self-help formats as well as the waiting list and care as usual control conditions. Rela-

tively few direct comparisons between individual, group, and guided self-help CBT were available. Telephone CBT was not strongly attached to the network, with a relatively small number of trials comparing it with individual therapy as well as with the waiting list and care as usual control conditions. Pill placebo was compared with only individual CBT in 2 trials and not with any other format or control condition; thus, no closed loops were found with pill placebo. Unguided self-help was compared with guided self-help CBT in a small number of studies as well as with the waiting list and care as usual control conditions but not with individual CBT. The contribution plot, showing the percentage of contributions from the direct comparisons for the mixed and indirect estimates, is presented in eAppendix E in the Supplement.

Pairwise Meta-analyses

Table 1 shows the results of the pairwise meta-analyses, consisting of 6 comparisons with more than 10 included studies (see the forest plots in eAppendix F in the Supplement). Individual, group, telephone, and guided self-help formats were more effective than the waiting list and care as usual control conditions. Furthermore, group therapy was statistically significantly less effective than individual therapy; unguided self-help therapy was significantly less effective than guided self-help but was more effective than being on a waiting list; and individual therapy was significantly more effective than taking pill placebo. None of the other comparisons was statistically significant (possibly owing to low power).

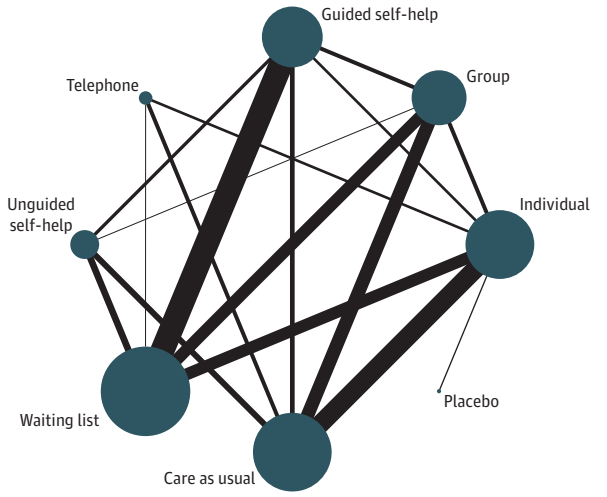
Heterogeneity was moderate to very high in all comparisons with more than 10 studies (range of I^2 statistic, 51%-92%) except for unguided self-help CBT compared with the waiting list control condition. Egger test was statistically significant for all 6 comparisons, including the waiting list or care as usual control condition (except the comparisons between guided self-help vs care as usual, telephone vs care as usual, and unguided self-help vs waiting list), suggesting substantial publication bias.

Network Meta-analysis

The main results of the network meta-analysis are presented in **Figure 2**. Indirect evidence could be calculated for the 9 comparisons for which no direct evidence was available. Individual, group, guided self-help, and telephone CBT were statistically significantly more effective than the unguided self-help CBT (SMD, 0.34-0.59) as well as the waiting list (SMD, 0.87-1.11) and care as usual (SMD, 0.47-72) control conditions. We found no statistically significant differences between individual, group, guided self-help, and telephone CBT except for a small but statistically significant superiority of group CBT over guided self-help CBT (SMD, 0.25). Unguided self-help CBT was more effective than the waiting list control condition (SMD, 0.52) but not more effective than the care as usual (SMD, 0.13) control condition. Pill placebo is not included in Figure 2 because it was examined in only 2 studies, and none of the results was statistically significant, which may be attributed to a lack of statistical power (see the results in eAppendix G in the Supplement).

Visual inspection of the distribution of potential effect modifiers (eAppendix H in the Supplement) indicated that these potential effect modifiers were similarly distributed across the comparisons in the network, suggesting no significant evidence against the transitivity assumption.

Figure 1. Network Plot of Meta-analysis



Consistency factors were examined using the loop-specific approach (eAppendix I in the Supplement). The highest inconsistency factor was found for the loop of group CBT, unguided self-help, and waiting list. However, no inconsistency factors were found to be statistically significant, although this finding cannot be considered as evidence of the absence of inconsistency because of low power in some of the loops, especially in the presence of large heterogeneity in pairwise comparisons. The design-by-treatment interaction model did not indicate global inconsistency in the network (τ^2_{25} = 23.70; *P* for the null hypothesis of consistency in the network = .54).

The certainty of evidence for each network estimate is reported in eAppendix J in the Supplement. Among the major comparisons, certainty of evidence was moderate for individual compared with guided self-help CBT and for guided self-help compared with telephone CBT, but it was low for the comparisons between individual CBT and care as usual control condition, group and guided self-help CBT, as well as telephone CBT and waiting list or care as usual control condition.

Acceptability

The outcomes of the network meta-analysis for acceptability are shown in Figure 2. No indications of statistically significant differences were found between individual, group, and telephone CBT. Guided self-help was statistically significantly less acceptable than individual (RR = 1.44; 95% CI, 1.09-1.89) and group (RR = 1.38; 95% CI, 1.06-1.80) therapies as well as the care as usual (RR = 0.72; 95% CI, 0.57-0.90) and waiting list (RR = 0.63; 95% CI, 0.52-0.75) control conditions. Unguided self-help was less acceptable than being on a waiting list (RR = 0.75; 95% CI, 0.62-0.91). Individual and telephone CBT were more acceptable than pill placebo (eAppendix G in

Table 1. Pairwise Meta-analyses of CBT Delivery Formats[a]

Format Comparison	No.	SMD (95% CI)	I^2 Statistic (95% CI)	tau^2	Egger Test *P* Value
Individual vs					
Group	7	−0.32 (−0.63 to −0.00)	24 (0-68)	0.04	.56
Guided self-help	4	−0.12 (−0.54 to 0.31)	6 (0-70)	0.01	.06
Telephone-administered	4	−0.04 (−0.30 to 0.22)	16 (0-73)	0.01	.13
Waiting list	18	−1.08 (−1.34 to −0.81)	53 (8-71)	0.16	.001
Care as usual	30	−0.52 (−0.65 to −0.39)	51 (18-67)	0.07	.22
Pill placebo	2	−0.40 (−0.68 to −0.11)	NC	0.00	NC
Group vs					
Guided self-help	5	0.20 (−0.08 to 0.49)	0 (0-64)	0.00	.95
Unguided self-help	1	−0.06 (−0.34 to 0.22)	NC	NC	NC
Waiting list	18	−1.32 (−1.72 to −0.91)	92 (89-94)	0.64	.02
Care as usual	21	−0.83 (−1.12 to −0.54)	88 (84-91)	0.39	.003
Guided self-help vs					
Unguided self-help	5	−0.37 (−0.55 to −0.18)	17 (0-70)	0.01	.55
Waiting list	35	−0.81 (−0.98 to −0.63)	74 (63-81)	0.19	.01
Care as usual	8	−0.56 (−0.82 to −0.30)	79 (52-88)	0.10	.19
Telephone vs					
Waiting list	1	−0.69 (−1.06 to −0.31)	NC	NC	NC
Care as usual	6	−0.63 (−1.07 to −0.19)	87 (71-92)	0.25	.85
Unguided self-help vs					
Waiting list	11	−0.48 (−0.60 to −0.18)	17 (0-59)	0.01	.31
Care as usual	9	−0.14 (−0.29 to 0.02)	57 (0-78)	0.03	.02

Abbreviations: CBT, cognitive behavior therapy; NC, not calculated; SMD, standardized mean difference.

[a] For the following comparisons, no studies were available: individual vs unguided self-help, group vs telephone, guided self-help vs telephone, telephone vs unguided self-help, waiting list vs care as usual, and any format (except individual) vs placebo.

Figure 2. Network Meta-analyses of Cognitive Behavior Therapy (CBT) Delivery Formats

Nodes examined | Effect sizes (SMDs) | Acceptability (RRs)

Individual	1.04 (0.80 to 1.35) [0.59 to 1.83]	**1.44 (1.09 to 1.89) [0.81 to 2.55]**	0.97 (0.71 to 1.33) [0.54 to 1.75]	1.19 (0.91 to 1.57) [0.67 to 2.11]	0.90 (0.70 to 1.16) [0.51 to 1.58]	1.03 (0.85 to 1.24) [0.60 to 1.75]
-0.09 (-0.32 to 0.13) [-1.15 to 0.97]	**Group**	**1.38 (1.06 to 1.80) [0.78 to 2.43]**	0.93 (0.64 to 1.35) [0.50 to 1.74]	1.14 (0.88 to 1.48) [0.65 to 2.01]	0.86 (0.68 to 1.09) [0.50 to 1.50]	0.99 (0.80 to 1.22) [0.57 to 1.70]
0.15 (-0.09 to 0.40) [-0.91 to 1.22]	**0.25 (0.01 to 0.49) [-0.82 to 1.31]**	**Guided Self-help**	0.68 (0.46 to 0.99) [0.36 to 1.27]	0.83 (0.66 to 1.05) [0.48 to 1.44]	**0.63 (0.52 to 0.75) [0.37 to 1.07]**	**0.72 (0.57 to 0.90) [0.41 to 1.24]**
0.00 (-0.38 to 0.37) [-1.11 to 1.10]	0.09 (-0.31 to 0.49) [-1.02 to 1.20]	-0.16 (-0.57 to 0.25) [-1.27 to 0.96]	**Telephone-Administered**	1.23 (0.84 to 1.79) [0.65 to 2.31]	0.93 (0.64 to 1.34) [0.50 to 1.73]	1.06 (0.77 to 1.45) [0.58 to 1.92]
0.50 (0.21 to 0.78) [-0.58 to 1.57]	**0.59 (0.30 to 0.88) [-0.48 to 1.66]**	**0.34 (0.07 to 0.61) [-0.73 to 1.41]**	**0.50 (0.07 to 0.94) [-0.62 to 1.62]**	**Unguided Self-help**	**0.75 (0.62 to 0.91) [0.44 to 1.29]**	0.86 (0.69 to 1.08) [0.50 to 1.50]
1.02 (0.80 to 1.24) [-0.04 to 2.08]	**1.11 (0.90 to 1.33) [0.06 to 2.17]**	**0.87 (0.69 to 1.04) [-0.18 to 1.92]**	**1.02 (0.63 to 1.42) [-0.09 to 2.13]**	**0.52 (0.28 to 0.77) [-0.54 to 1.59]**	**Waiting List**	1.14 (0.92 to 1.42) [0.66 to 1.98]
0.63 (0.45 to 0.80) [-0.42 to 1.68]	**0.72 (0.52 to 0.92) [-0.33 to 1.77]**	**0.47 (0.25 to 0.70) [-0.59 to 1.53]**	**0.63 (0.27 to 1.00) [-0.47 to 1.73]**	0.13 (-0.13 to 0.39) [-0.94 to 1.20]	**-0.39 (-0.60 to -0.18) [-1.45 to 0.66]**	**Care as Usual**

The diagonal gives the different nodes that were examined in the study; at the left of the diagonal, the data for the effect sizes are given as standardized mean difference (SMD) with 95% CIs and 95% prediction intervals, with every cell indicating the values for a specific contrast between the nodes. At the right of the diagonal, the values for acceptability are given as relative risk (RR) with 95% CIs and 95% prediction intervals. Data in bold are statistically significant. Pill placebo is not included because only 2 studies used a pill placebo condition and both compared placebo with individual CBT. The results including pill placebo are presented in eAppendix G in the Supplement.

the Supplement), but placebo was only examined in 2 studies and thus should be considered with caution.

Ranking of Treatment Formats

The results of the analyses on the ranking of treatment formats (surface under the cumulative ranking curve) are shown in **Table 2** separately for the efficacy and for the acceptability. In the **Figure 3** forest plot, the treatment formats are ranked, with care as usual as the reference group. Individual (77.6%; SMD, -0.63), group (90.5%; SMD, -0.72), telephone (76.8%; SMD, -0.63), and guided self-help (55.8%; SMD, -0.47) formats ranked best with small differences. For acceptability, telephone CBT had the highest ranking, followed by individual, group, and unguided self-help therapies. Guided self-help format ranked considerably lower than the other treatment formats (1.6%; RR = 0.72).

Long-term Effectiveness

The results of the network meta-analysis at 3 to 12 months of follow-up are presented in eAppendix K in the Supplement. The network was not well populated, with 14 of the 21 comparisons having 2 or fewer effect sizes (7 comparisons had no effect size) and with only 2 comparisons having more than 10 effect sizes. Only 3 studies were available for telephone CBT and 2 studies for the waiting list control condition. The design-by-treatment interaction model did not indicate global inconsistency in the network (τ^2_{13} = 10.70; *P* for the null hypothesis of consistency in the network = .64). The results of the network meta-analysis suggested positive and statistically significant effectiveness of individual, group, guided self-help, and telephone CBT compared with the care as usual control condition. Telephone CBT was also more effective than the waiting list and unguided self-help but less effective than individual CBT. However, because of the small number of comparisons, especially on telephone CBT, all of these findings have to be considered with caution.

The results of the meta-regression analyses are reported in eAppendix L in the Supplement. Only 1 predictor was found to be statistically significant. Because of the correlational nature of these findings, the large number of analyses conducted, and the relatively high *P* values for the statistically significant result (ie, *P* > .01), these results should be interpreted with caution.

Sensitivity Analyses

In the first sensitivity analysis (limited to studies with low risk of bias; eAppendix M in the Supplement), the network was not well populated. The results were, however, comparable to the overall results, with statistically significant differences between individual, group, guided self-help, and telephone CBT on the one hand and the care as usual control condition on the other hand. Individual, group, and guided self-help (but not telephone) formats were significantly more effective than the waiting list control condition. Unguided self-help CBT was significantly more effective than the waiting list but not care as usual. In the second sensitivity analysis (with the outliers excluded; eAppendix N in the Supplement), the results were again comparable to the main analyses.

In the third sensitivity analysis, we included only internet-based guided and unguided CBT and excluded other types of self-help therapy (see eAppendixes O and P in the Supplement for effectiveness and acceptability). Again, the results were comparable to findings in the main analyses, with individual, group, guided self-help, and telephone CBT being statistically significantly more effective than care as usual, waiting list, and unguided self-help. Acceptability was significantly lower in guided self-help compared with other treatment formats.

Discussion

The results of this network meta-analysis suggest that individual, group, telephone-administered, and guided self-help (internet-based or not) treatment formats have comparable effectiveness in the treatment of depression and that the effectiveness does not differ statistically significantly across formats. The effect sizes of these treatment formats compared with the care as usual control condition were moderate or large when compared with the waiting list control condition. Although guided self-help CBT was as effective as individual, group, and telephone CBT, it was less acceptable as the other formats. This finding was statistically significant when guided self-help was compared with individual and group CBT.

Table 2. Ranking of CBT Delivery Formats by Surface Under the Cumulative Ranking Curve

CBT Format	Effectiveness, %	Acceptability, %
Individual	77.6	62.5
Group	90.5	51.8
Guided self-help	55.8	1.6
Telephone-administered	76.8	67.7
Unguided self-help	30.9	24.3
Waiting list	0	87.5
Care as usual	19.5	54.6

Abbreviation: CBT, cognitive behavior therapy.

We also found that unguided self-help (without any involvement of a therapist) was statistically significantly less effective than that of individual, group, telephone, and guided self-help CBT. Unguided CBT was more effective than the waiting list but not the care as usual control condition. All results were broadly confirmed in several sensitivity analyses.

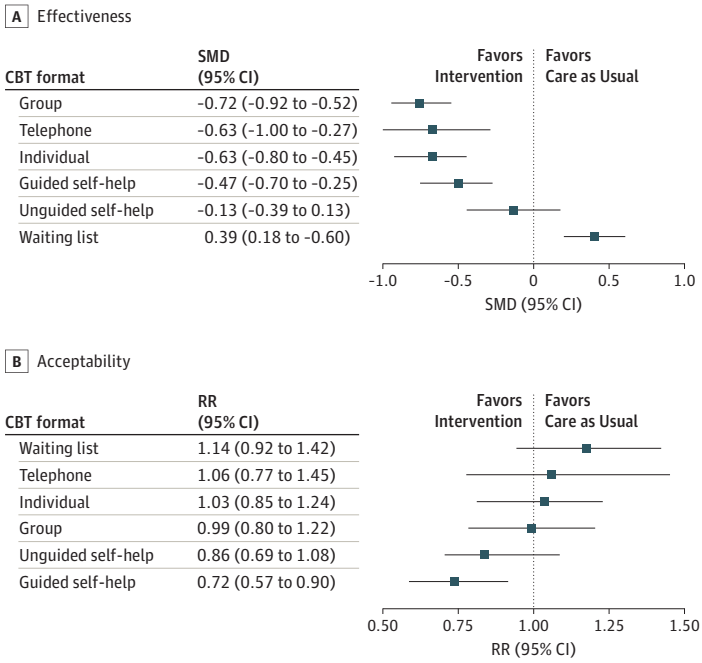
Although these findings are in line with results of previous meta-analytic research confirming the comparable effectiveness of individual, group, telephone, and self-help CBT, this current network meta-analysis (which includes the largest number of studies in the field, to our knowledge) takes advantage of all direct and indirect comparisons simultaneously, thus making the estimates more precise and consistent. To our knowledge, this network meta-analysis is the first to compare alternative delivery formats at the same time and on a common metric. An earlier meta-analysis found that individual therapies were more effective than group therapy.[10] Our pairwise comparisons between individual and group therapies supported this finding, but in the network meta-analysis, no significant difference was found. This result suggests that a small difference may exist between individual and group therapy but that more high-quality research is needed to examine this issue.

It is not clear why the acceptability of guided self-help CBT was lower compared with that for the other formats. Maybe the absence of direct contact with a professional makes it easier to stop the treatment because there is less personal-relationship pressure to continue with the treatment or the study. However, lower acceptability would then also be expected to happen in unguided CBT, which we did not find. More research is needed to examine this issue.

Limitations

This study has several limitations that should be taken into consideration when interpreting the results. First, not enough

Figure 3. Ranked Forest Plots of Effectiveness and Acceptability of Cognitive Behavior Therapy (CBT) Formats



Care-as-usual format is the reference group for both the effectiveness (A) and acceptability (B) plots. RR indicates relative risk; SMD, standardized mean difference.

studies on placebo were available from which to draw any conclusions about comparisons with placebo. Furthermore, relatively few studies examined the effectiveness of telephone CBT, although they suggested that telephone CBT was comparable to individual and group CBT both in terms of efficacy and acceptability. Second, substantial heterogeneity was found in several of the examined comparisons. We defined CBT as a psychological treatment in which cognitive restructuring was one of the core elements. However, most treatments also included other components, such as behavioral activation, problem solving, mindfulness, and social skills training. The variety of components included in these treatments differed widely, which may have contributed to the statistical heterogeneity and certainly to the clinical heterogeneity. We did not find indications of significant inconsistency, however.

Third, we could examine whether our findings were valid across different categories of baseline severity because baseline severity was measured with many different instruments. We found no indication that the transitivity assumption was violated in this study, but it is important to conduct more research on the differences between groups of patients, such as those who use internet-based treatments and those who do not as well as those who use guided self-help and those who use unguided interventions. Fourth, although network meta-analyses make optimal use of all available data, the indirect evidence is not directly based on randomized clinical trials.[34] Fifth, we found indications of publication bias in several analyses, although our analyses suggested comparable results after adjustment for publication bias, possibly because such bias existed only between active and control conditions and therefore did not affect the relative efficacy among the active interventions. The same was true for risk of bias, with the sample of studies having considerable risk of bias and with sensitivity analyses suggesting comparable results in studies with low risk of bias.

Conclusions

This study suggests that group, telephone, and guided self-help treatments are effective interventions that may be considered as alternatives to individual CBT. Applying effective and acceptable CBT in a range of different formats will make CBT easier to implement, disseminate, and deliver across different settings and diverse patient populations. These results should inform future clinical guidelines worldwide for the management of depression.

ARTICLE INFORMATION

Accepted for Publication: January 23, 2019.

Published Online: April 17, 2019. doi:10.1001/jamapsychiatry.2019.0268

Correction: This article was corrected on July 17, 2019, to fix an error in Figure 3.

Author Affiliations: Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health Research Institute, Vrije Universiteit Amsterdam, the Netherlands (Cuijpers); Department of Data Science, The Institute of Statistical Mathematics, Tokyo, Japan (Noma, Karyotaki); Department of Psychiatry, Warneford Hospital, University of Oxford, Oxford, United Kingdom (Cipriani); Oxford Health NHS Foundation Trust, Warneford Hospital, Oxford, United Kingdom (Cipriani); Department of Health Promotion and Human Behavior, Kyoto University Graduate School of Medicine, School of Public Health, Kyoto, Japan (Furukawa).

Author Contributions: Dr Cuijpers had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Cuijpers, Karyotaki, Cipriani.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Cuijpers.
Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Cuijpers, Noma, Karyotaki, Cipriani.
Administrative, technical, or material support: Cipriani.

Conflict of Interest Disclosures: Dr Noma reported personal fees from Boehringer Ingelheim, Kyowa Hakko Kirin, and ASKA Pharmaceutical outside of the submitted work. Dr Cipriani reported support from the National Institute for Health Research (NIHR) Oxford Cognitive Health Clinical Research Facility, professorship grant RP-2017-08-ST2-006 from the NIHR Research, and grant BRC-1215-20005 from the NIHR Oxford Health Biomedical Research Centre. Dr Furukawa reported personal fees from Meiji Seika Pharma, grants and personal fees from Mitsubishi-Tanabe, personal fees from MSD, and personal fees from Pfizer outside of the submitted work and a pending patent to 2018-177688. No other disclosures were reported.

Disclaimer: The views expressed herein are those of the authors and do not necessarily reflect those of the UK National Health Service, the National Institute for Health Research, or the UK Department of Health.

REFERENCES

1. Barth J, Munder T, Gerger H, et al. Comparative efficacy of seven psychotherapeutic interventions for patients with depression: a network meta-analysis. *PLoS Med*. 2013;10(5):e1001454. doi:10.1371/journal.pmed.1001454

2. Cuijpers P, Berking M, Andersson G, Quigley L, Kleiboer A, Dobson KS. A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *Can J Psychiatry*. 2013;58(7):376-385. doi:10.1177/070674371305800702

3. Cuijpers P, van Straten A, Andersson G, van Oppen P. Psychotherapy for depression in adults: a meta-analysis of comparative outcome studies. *J Consult Clin Psychol*. 2008;76(6):909-922. doi:10.1037/a0013075

4. Beck AT, Rush AJ, Shaw BF, Emery G. *Cognitive Therapy of Depression*. New York, NY: The Guilford Press; 1979.

5. Feng C-Y, Chu H, Chen C-H, et al. The effect of cognitive behavioral group therapy for depression: a meta-analysis 2000-2010. *Worldviews Evid Based Nurs*. 2012;9(1):2-17. doi:10.1111/j.1741-6787.2011.00229.x

6. Huntley AL, Araya R, Salisbury C. Group psychological therapies for depression in the community: systematic review and meta-analysis. *Br J Psychiatry*. 2012;200(3):184-190. doi:10.1192/bjp.bp.111.092049

7. Okumura Y, Ichikura K. Efficacy and acceptability of group cognitive behavioral therapy for depression: a systematic review and meta-analysis. *J Affect Disord*. 2014;164:155-164. doi:10.1016/j.jad.2014.04.023

8. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cogn Behav Ther*. 2009;38(4):196-205. doi:10.1080/16506070903318960

9. Karyotaki E, Riper H, Twisk J, et al. Efficacy of self-guided internet-based cognitive behavioral therapy in the treatment of depressive symptoms: a meta-analysis of individual participant data. *JAMA Psychiatry*. 2017;74(4):351-359. doi:10.1001/jamapsychiatry.2017.0044

10. Cuijpers P, van Straten A, Warmerdam L. Are individual and group treatments equally effective in the treatment of depression in adults? a meta-analysis. *Eur J Psychiatry*. 2008;22(1):38-51. doi:10.4321/S0213-61632008000100005

11. Burlingame GM, Seebeck JD, Janis RA, et al. Outcome differences between individual and group formats when identical and nonidentical treatments, patients, and doses are compared: a 25-year meta-analytic perspective. *Psychotherapy (Chic)*. 2016;53(4):446-461. doi:10.1037/pst0000090

12. Cuijpers P, Donker T, van Straten A, Li J, Andersson G. Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? a systematic review and meta-analysis of comparative outcome studies. *Psychol Med*. 2010;40(12):1943-1957. doi:10.1017/S0033291710000772

13. Andersson G, Cuijpers P, Carlbring P, Riper H, Hedman E. Guided internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry*. 2014;13(3):288-295. doi:10.1002/wps.20151

14. Carlbring P, Andersson G, Cuijpers P, Riper H, Hedman-Lagerlöf E. Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. *Cogn Behav Ther*. 2018;47(1):1-18. doi:10.1080/16506073.2017.1401115

15. Higgins JPT, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. doi:10.1136/bmj.d5928

16. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23(1):56-62. doi:10.1136/jnnp.23.1.56

17. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4(6):561-571. doi:10.1001/archpsyc.1961.01710120031004

18. Beck AT, Steer RA, Brown GK. *BDI-II. Beck Depression Inventory*. 2nd ed. San Antonio, TX: Psychological Corporation; 1996.

19. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613. doi:10.1046/j.1525-1497.2001.016009606.x

20. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1(3):385-401. doi:10.1177/014662167700100306

21. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*. 1983;67(6):361-370. doi:10.1111/j.1600-0447.1983.tb09716.x

22. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet*. 2018;391(10128):1357-1366. doi:10.1016/S0140-6736(17)32802-7

23. Ioannidis JPA, Patsopoulos NA, Evangelou E. Uncertainty in heterogeneity estimates in meta-analyses. *BMJ*. 2007;335(7626):914-916. doi:10.1136/bmj.39343.408449.80

24. Orsini N, Bottai M, Higgins J, Buchan I. Heterogi: Stata module to quantify heterogeneity in a meta-analysis. *Statistical Software Components*. https://ideas.repec.org/c/boc/bocode/s449201.html. Revised January 25, 2006. Accessed March 14, 2019.

25. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med*. 2015;162(11):777-784. doi:10.7326/M14-2385

26. Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Stat Methods Med Res*. 2008;17(3):279-301. doi:10.1177/0962280207080643

27. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods*. 2012;3(2):80-97. doi:10.1002/jrsm.1037

28. Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One*. 2013;8(10):e76654. doi:10.1371/journal.pone.0076654

29. Higgins JPT, Jackson D, Barrett JK, Lu G, Ades AE, White IR. Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. *Res Synth Methods*. 2012;3(2):98-110. doi:10.1002/jrsm.1044

30. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JP. Evaluating the quality of evidence from a network meta-analysis. *PLoS One*. 2014;9(7):e99682. doi:10.1371/journal.pone.0099682

31. CINeMA [computer program]. Version 1.4.1. http://cinema.ispm.ch/. Accessed October 10, 2018.

32. Gilbody S, Littlewood E, Hewitt C, et al; REEACT Team. Computerised cognitive behaviour therapy (cCBT) as treatment for depression in primary care (REEACT trial): large scale pragmatic randomised controlled trial. *BMJ*. 2015;351:h5627. doi:10.1136/bmj.h5627

33. Vernmark K, Lenndin J, Bjärehed J, et al. Internet administered guided self-help versus individualized e-mail therapy: a randomized trial of two versions of CBT for major depression. *Behav Res Ther*. 2010;48(5):368-376. doi:10.1016/j.brat.2010.01.005

34. Chaimani A, Salanti G, Leucht S, Geddes JR, Cipriani A. Common pitfalls and mistakes in the set-up, analysis and interpretation of results in network meta-analysis: what clinicians should look for in a published article. *Evid Based Ment Health*. 2017;20(3):88-94. doi:10.1136/eb-2017-102753